

*R  
C  
and*

in Table 3] by comparison of a part of the NS5 gene nucleotide sequence spanning positions 7932 to 8271, [with said amino acid numbering being shown in Table 1,] and with said polynucleic acid containing at least one nucleotide differing from said known HCV nucleotide sequences, or the complement thereof.

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4. The [A] polynucleic acid according to [any of] claim[s] 1 [to 3] encoding an HCV polyprotein comprising in its amino acid sequence at least one of the following amino acid residues:

I15, C38, V44, A49, Q43, P49, Q55, A58, S60 or D60, E68 or V68, H70, A71 or Q71 or N71, D72, H81, H101, D106, S110, L130, I134, E135, L140, S148, T150 or E150, Q153, F155, D157, G160, E165, I169, F181, L186, T190, T192 or I192 or H192, I193, A195, S196, R197 or N197 or K197, Q199 or D199 or H199 or N199, F200 or T200, A208, I213, M216 or S216, N217 or S217 or G217 or K217, T218, I219, A222, Y223, I230, W231 or L231, S232 or H232 or A232, Q233, E235 or L235, F236 or T236, F237, L240 or M240, A242, N244, N249, I250 or K250 or R250, A252 or C252, A254, I255 or V255, D256 or M256, E257, E260 or K260, R261, V268, S272 or R272, I285, G290 or F290, A291, A293 or W293, T294 or A294, S295 or H295, K296 or E296, Y297 or M297, I299 or Y299, I300, S301, P316, S2646, A2648, G2649, A2650, V2652, Q2653, H2656 or L2656, D2657, E2659, K2663 or Q2663, A2667 or V2667, D2677, L2681, M2686 or Q2686 or E2686, A2692 or K2692, H2697, I2707, L2708 or Y2708, A2709, A2719 or M2719, F2727, T2728 or D2728, E2729, F2730 or Y2730, I2741, I2745, V2746 or E2746 or L2746 or K2746, A2748, S2749 or P2749, R2750, E2751, D2752 or N2752 or S2752 or T2752 or V2752 or I2752 or Q2752, S2753 or D2753 or G2753, D2754, A2755, L2756 or Q2756, R2757,

with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering as shown in Table 1, or a part of said polynucleic acid which is unique to at least one of the HCV subtypes or types as defined in claim[s] 2 to 3] 1, and which contains at least one nucleotide differing from known HCV nucleotide sequences, or the complement thereof.

5. The [A] polynucleic acid according to [any of] claim[s] 1 [to 4], with said polynucleic acid encoding a HCV polyprotein comprising in its amino acid sequence at least one amino acid sequence chosen from the following list:

|   |                                  |
|---|----------------------------------|
| ARQSDGRSWAQ or ARRSEGRSWAQ as for subtype 1d                                      | (SEQ ID NO 107 and 108)          |
| ERRPEGRSWAQ as for subtype 1e   | (SEQ ID NO 109)                  |
| ARRPEGRSWAQ as for subtype 1f   | (SEQ ID NO 110)                  |
| DRRTTGKSWGR as for subtype 2k   | (SEQ ID NO 111)                  |
| DRRATGRSWGR as for subtype 2e   | (SEQ ID NO 112)                  |
| DRRATGKSWGR as for subtype 2f   | (SEQ ID NO 113)                  |
| VRQPTGRSWGQ as for type 9   | (SEQ ID NO 114)                  |
| VRHQTGRTWAQ as for subtype 7a and 7c  | (SEQ ID NO 115)                  |
| VRQNQGRTWAQ as for subtype 7d   | (SEQ ID NO 116)                  |
| ARRTEGRSWAQ as for type 10  | (SEQ ID NO 117)                  |
| VRRTTGRXXXX or VRRTTGRWTWAQ as for type 11  | (SEQ ID NO 118 and 119)          |
| HEVRNASGVYHVA or HEVRNASGVYHL as for subtype 1d                                   | (SEQ ID NO 120 and 121)          |
| ARQSDGRSWAQ or ARRSEGRSWAQ as for subtype 1d                                      | (SEQ ID NO 107 and 108)          |
| ERRPEGRSWAQ as for subtype 1e   | (SEQ ID NO 109)                  |
| ARRPEGRSWAQ as for subtype 1f   | (SEQ ID NO 110)                  |
| DRRTTGKSWGR as for subtype 2k   | (SEQ ID NO 111)                  |
| DRRATGRSWGR as for subtype 2e   | (SEQ ID NO 112)                  |
| DRRATGKSWGR as for subtype 2f   | (SEQ ID NO 113)                  |
| VRQPTGRSWGQ as for type 9   | (SEQ ID NO 114)                  |
| VRHQTGRTWAQ as for subtype 7a and 7c  | (SEQ ID NO 115)                  |
| VRQNQGRTWAQ as for subtype 7d   | (SEQ ID NO 116)                  |
| ARRTEGRSWAQ as for type 10  | (SEQ ID NO 117)                  |
| VRRTTGRXXXX or VRRTTGRWTWAQ as for type 11  | (SEQ ID NO 118 and 119)          |
| HEVRNASGVYHVA or HEVRNASGVYHL as for subtype 1d                                   | (SEQ ID NO 120 and 121)          |
| YEVHSTTDGYHV as for subtype 1f  | (SEQ ID NO 122)                  |
| VEVKNTSQAYMA as for subtype 2e  | (SEQ ID NO 123)                  |
| IQVKNNSHFYMA as for subtype 2f  | (SEQ ID NO 124)                  |
| VQVKNTSTMYMA as for subtype 2g  | (SEQ ID NO 126)                  |
| VQVANR8GSYMV as for subtype 2i  | (SEQ ID NO 127)                  |
| VEIKNTXNTYVL or VEIKNTSNTYVL as for subtype 2k                                    | (SEQ ID NO 128 and 129)          |
| INYRNVSGIYYY or INYRNTSGIYHV<br>or INYHNTSGIYHI or TYYRNVSGIYHV as for subtype 4k | (SEQ ID NO 130, 131, 132 or 133) |
| QHYRNVSGIYHV as for subtype 4l  | (SEQ ID NO 134)                  |
| IQVKNASGIYHL as for type 9  | (SEQ ID NO 135)                  |

|  |                                     |
|--|-------------------------------------|
| AHYTNKSGLYHL as for subtype 7c   | (SEQ ID NO 136)                     |
| LNYANKSGLYHL as for subtype 7d   | (SEQ ID NO 137)                     |
| LEYRNASGLYLMV as for type 10   | (SEQ ID NO 138)                     |
| IYEMDGMIHY or IYEMMSGMILHA as for subtype 1d   | (SEQ ID NO 139 and 140)             |
| VYEAKDIILHT as for subtype 1f  | (SEQ ID NO 141)                     |
| VWQLXDAVLHV as for subtype 2e  | (SEQ ID NO 142)                     |
| VWQLRDAVLHV as for subtype 2f  | (SEQ ID NO 143)                     |
| IWQMKGAVLHV as for subtype 2g  | (SEQ ID NO 144)                     |
| VWQLKDAVLHV as for subtype 2h  | (SEQ ID NO 145)                     |
| VWQLEEAVLHV as for subtype 2i  | (SEQ ID NO 146)                     |
| TWQLXXAVLHV as for subtype 2k  | (SEQ ID NO 147)                     |
| VYEADHHILHL or VYEADHHILAL<br>or VFEADHHILHL as for subtype 4k   | (SEQ ID NO 148, 149 and 150)        |
| VYESDHILHL as for subtype 41   | (SEQ ID NO 151)                     |
| VFEAETMILHL as for type 9  | (SEQ ID NO 152)                     |
| VYEAEYLILHL as for subtype 7c  | (SEQ ID NO 153)                     |
| VYEANGMILHL as for subtype 7d  | (SEQ ID NO 154)                     |
| VYEAGDIILHL as for type 10   | (SEQ ID NO 155)                     |
| VREDNHLCWMAL or VRENNSSRCWMAL as for subtype 1d  | (SEQ ID NO 156 and 157)             |
| IREGNISRCWVPL as for subtype 1f  | (SEQ ID NO 158)                     |
| ENSSGRFHCWIPI as for subtype 2e  | (SEQ ID NO 159)                     |
| ERSGNRTFCWTAV as for subtype 2f  | (SEQ ID NO 160)                     |
| ELQGNKSRCWIPV as for subtype 2g  | (SEQ ID NO 162)                     |
| ERHQNQSRCWIPV as for subtype 2h  | (SEQ ID NO 163)                     |
| EWKDNTSRCWIPV as for subtype 2i  | (SEQ ID NO 164)                     |
| EREGNSSRCWIPV as for subtype 2k  | (SEQ ID NO 165)                     |
| VREGNQSRCWVAL or VRTGNQSRCWVAL<br>or VRVGNQSSCWVAL VRVGNQSRCWVAL or VKEGNKSRCWVAL<br>as for subtype 4k | (SEQ ID NO 166, 167, 168<br>or 169) |
| VKTGNTSRCWVAL as for subtype 41  | (SEQ ID NO 170)                     |
| IKAGNESRCWLPV as for type 9  | (SEQ ID NO 171)                     |
| VKEGNQSRCWVQA as for subtype 7c  | (SEQ ID NO 172)                     |
| VKXXNLTKCWLSA as for subtype 7d  | (SEQ ID NO 173)                     |
| VRSGNTSRCWIPV as for type 10   | (SEQ ID NO 174)                     |
| VKNASVPTAA or VKDANVPTAA as for subtype 1d   | (SEQ ID NO 175 and 176)             |
| ARIANAPIDE as for subtype 1f   | (SEQ ID NO 177)                     |
| VSKPGALTG as for subtype 2e  | (SEQ ID NO 178)                     |
| VSRPGALTRG as for subtype 2f   | (SEQ ID NO 179)                     |

|  |                                     |
|--|-------------------------------------|
| VNQPGALTRG as for subtype 2g   | (SEQ ID NO 180)                     |
| VSQPGALTRG as for subtype 2h   | (SEQ ID NO 181)                     |
| VSQPGALTG as for subtype 2i  | (SEQ ID NO 182)                     |
| VSRPGALTEG as for subtype 2k   | (SEQ ID NO 183)                     |
| APYIGAPLES or APYTAAPLES as for subtype 4k                               | (SEQ ID NO 184 and 185)             |
| APILSAPLMS as for subtype 4l   | (SEQ ID NO 186)                     |
| VPNSSVPIHG as for type 9   | (SEQ ID NO 187)                     |
| VPNASTPVTG as for subtype 7c   | (SEQ ID NO 188)                     |
| VQNASVSIRG as for subtype 7d   | (SEQ ID NO 189)                     |
| VKSPCAATAS as for type 10  | (SEQ ID NO 190)                     |
| SPRMHHTTQE or SPRYLHHTTQE as for subtype 1d                              | (SEQ ID NO 191 and 192)             |
| TSRRHWTQD as for subtype 1f  | (SEQ ID NO 193)                     |
| APKRHYFVQE as for subtype 2e   | (SEQ ID NO 194)                     |
| SPQYHTFVQE as for subtype 2f   | (SEQ ID NO 195)                     |
| SPQHHNFSQD as for subtype 2g   | (SEQ ID NO 196)                     |
| SPQHHIFVQD as for subtype 2h   | (SEQ ID NO 197)                     |
| SPEHHHFVQD as for subtype 2k   | (SEQ ID NO 198)                     |
| RPRRHWTTQD or RPRRHWTAQD or<br>QPRRHWTQD or RPRRHWTTQE as for subtype 4k | (SEQ ID NO 199, 200,<br>201 or 202) |
| QPRRHWTQD as for subtype 4l  | (SEQ ID NO 203)                     |
| RPKYHQVTQD as for type 9   | (SEQ ID NO 204)                     |
| RPRMHQVVQE as for subtype 7c   | (SEQ ID NO 205)                     |
| RPRMYEIAQD as for subtype 7d   | (SEQ ID NO 206)                     |
| RHRQHWTVQD as for type 10  | (SEQ ID NO 207)                     |

or a part of said polynucleic acid which is unique to at least one of the HCV subtypes or types as defined in claim[s 2 to 3] 1, and which contains at least one nucleotide differing from known HCV nucleotide sequences, or the complement thereof.

6. The [A] polynucleic acid according to [any of] claim[s] 1 [to 5] having a sequence selected from any of SEQ ID NO 1 to 105, or a part of said polynucleic acid which is unique to at least one of the HCV subtypes or types as defined in claim[s 2 to 3] 1, and which contains at least one nucleotide differing from known HCV nucleotide sequences, or the complement thereof.

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7. The [A] polynucleic acid according to [any of] claim[s] 1 [to 6], which codes for the 5' UR, the Core/E1, the NS4 or the NS5B region, [or] a part thereof, or the complement thereof.

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9. An oligonucleotide primer comprising part of a polynucleic acid according to any of claims 1, 4, 5, 6 or 7 [to 8], with said primer being able to act as primer for specifically amplifying the nucleic acid of a certain isolate belonging to the genotype from which the primer is derived.

10. An oligonucleotide probe comprising part of a polynucleic acid according to any of claims 1, 4, 5, 6 or 7 [to 8], with said probe being able to act as a hybridization probe for specific detection and/or classification into types and/or subtypes of a HCV nucleic acid containing said nucleotide sequence, with said probe being possibly labeled or attached to a solid substrate.

13. The [A] diagnostic kit according to claim 12, wherein said probe(s) is(are) attached to a solid substrate.

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14. The [A] diagnostic kit according to claim 13, wherein a range of said probes are attached to specific locations on a solid substrate.

15. The [A] diagnostic kit according to claim 14, wherein said solid support is a membrane strip and said probes are coupled to the membrane in the form of parallel lines.

21. The [A] method according to claims 16 to 18, wherein said nucleic acids are labeled during or after amplification.

22. A polypeptide having an amino acid sequence encoded by a polynucleic acid according to [any of] claim[s] 1 [to 8], or a part thereof which is unique to at least one of the HCV subtypes or types as defined in claim[s] 2 or 3 1, and which contains at least one amino acid differing from any of the known HCV types or subtypes amino acid sequences, or an analog thereof being substantially homologous and biologically equivalent.

23. The [A] polypeptide according to claim 22 comprising in its amino acid sequence at least one of the following amino acid residues:

I15, C38, V44, A49, Q43, P49, Q55, A58, S60 or D60, E68 or V68, H70, A71 or Q71 or N71, D72, H81, H101, D106, S110, L130, I134, E135, L140, S148, T150 or E150, Q153, F155, D157, G160, E165, I169, F181, L186, T190, T192 or I192 or H192, I193, A195, S196, R197 or N197 or K197, Q199 or D199 or H199 or N199, F200 or T200, A208, I213, M216 or S216, N217 or S217 or G217 or K217, T218, I219, A222, Y223, I230, W231 or L231, S232 or H232 or A232, Q233, E235 or L235, F236 or T236, F237, L240 or M240, A242, N244, N249, I250 or K250 or R250, A252 or C252, A254, I255 or V255, D256 or M256, E257, E260 or K260, R261, V268, S272 or R272, I285, G290 or F290, A291, A293 or W293, T294 or A294, S295 or H295, K296 or E296, Y297 or M297, I299 or Y299, I300, S301, P316, S2646, A2648, G2649, A2650, V2652, Q2653, H2656 or L2656, D2657, F2659, K2663 or Q2663, A2667 or V2667, D2677, L2681, M2686 or Q2686 or E2686, A2692 or K2692, H2697, I2707, L2708 or Y2708, A2709, A2719 or M2719, F2727, T2728 or D2728, E2729, F2730 or Y2730, I2741, I2745, V2746 or E2746 or L2746 or K2746, A2748, S2749 or P2749, R2750, E2751, D2752 or N2752 or S2752 or T2752 or V2752 or I2752 or Q2752, S2753 or D2753 or G2753, D2754, A2755, L2756 or Q2756, R2757,

with said notation being composed of a letter representing the amino acid residue by its one-letter code, and a number representing the amino acid numbering as shown in Table 1, or a part of said

polynucleic acid which is unique to at least one of the HCV subtypes or types as defined in claim[s 2 to 3] 1, and which contains at least one nucleotide differing from known HCV nucleotide sequences, or the complement thereof.

24. The [A] polypeptide according to claim 22 comprising in its amino acid sequence at least one of the sequences represented by SEQ ID NO 107 to 207 as listed in claim 5, or part of said polypeptide which is unique to at least one of the HCV subtypes or types as defined in claim[s 2 to 3] 1, and which contains at least one amino acid differing from known HCV types or subtypes amino acid sequences, or an analog thereof being substantially homologous and biologically equivalent to said polypeptide.

25. The [A] polypeptide having an amino acid sequence as represented in any of SEQ ID NO 1 TO 106, or a part thereof which is unique to at least one of the HCV subtypes or types as defined in claim[s 2 to 3] 1, and which contains at least one amino acid differing from known HCV types or subtypes amino acid sequences, or an analog thereof being substantially homologous and biologically equivalent to said polypeptide.

26. The [A recombinant] polypeptide [encoded by a polynucleic acid] according to any of claims 1, 4, 5, 6 or 7 which is recombinantly produced [to 8, or a part thereof which is unique to at least one of the HCV subtypes or types as defined in claims 2 or 3, and which contains at least one amino acid differing from known HCV types or subtypes amino acid sequences, or an analog thereof being substantially homologous and biologically equivalent to said polypeptide].

27. A method for product of a recombinant polypeptide of claim 26, comprising:

- transformation of an appropriate cellular host with a recombinant vector, in which a polynucleic acid or a part thereof according to any of claims 1, 4, 5, 6, or 7 [to 8] has been inserted under the control of the appropriate regulatory elements,
- culturing said transformed cellular host under conditions enabling the expression of said insert, and,

- harvesting said polypeptide.

*AS  
Cont*

28. A recombinant expression vector comprising a polynucleic acid or a part thereof according to any of claims 1, 4, 5, 6 or 7 [to 8] operably linked to prokaryotic, eukaryotic, or viral transcription and translation control elements.

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30. A method for detecting antibodies to HCV present in a biological sample, comprising:

- contacting the biological sample to be analyzed for the present of HCV with a polypeptide according to any of claims 22 to [26] 25,
- detecting the immunological complex formed between said antibodies and said polypeptide.

31. A method for HCV typing, comprising:

- contacting the biological sample to be analyzed for the presence of HCV with a polypeptide according to any of claims 22 to [26] 25.
- detecting the immunological complex formed between said antibodies and said polypeptide.

32. A diagnostic kit for use in detecting the presence of HCV, said kit comprising at least one polypeptide according to any of claims 22 to [26] 25, with said polypeptide being possibly bound to a solid support.

33. A diagnostic kit for HCV typing, said kit comprising at least one polypeptide according to any of claims 22 to [26] 25, with said polypeptide being possibly bound to a solid support.

34. The [A] diagnostic kit according to claims 32 [to] or 33, said kit comprising a range of polypeptides which are attached to specific locations on a solid substrate.

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35. The [A] diagnostic kit according to claim[s 32 to] 34, wherein said solid support is a membrane strip and said polypeptides are coupled to the membrane in the form of parallel lines.

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36. A pharmaceutical composition comprising at least one polypeptide according to any of claims 22 to [26] 25 and a suitable excipient, diluent or carrier.

*A<sup>f</sup>*

39. A vaccine for immunizing a mammal against HCV infection, comprising at least one polypeptide according to claims 22 to [26] 25, in a pharmaceutically acceptable carrier.

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41. A peptide corresponding to an amino acid sequence encoded by at least one of the HCV polynucleic acids according to any of claims 1, 4, 5, 6 or 7 [to 8], with said peptide comprising an epitope being unique to at least one of the HCV subtypes or types as defined in claim[s 2 or 3] 1, and with said peptide containing at least one amino acid differing from any of the known HCV types or subtypes amino acid sequences, or an analog thereof being substantially homologous and biologically equivalent.

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46. The [A] diagnostic kit according to claims 44 or 45, wherein said peptides are selected from the following list:

- at least one NS4 peptide,
- at least one NS4 peptide and at least one Core peptide,
- at least one NS4 peptide and at least one Core peptide and at least one E1 peptide or,
- at least one NS4 peptide and at least one E1 peptide.

47. The [A] diagnostic kit according to claims 44 [to 46] or 45, said kit comprising a range of peptides which are attached to specific locations on a solid substrate.

48. The [A] diagnostic kit according to claims 44 [to 47] or 45, wherein said solid support is a membrane strip and said peptides are coupled to the membrane in the form of parallel lines.